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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,157	04/25/2001	Koichi Nishigaki	P66602US0	4171

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EXAMINER
GUNTER, DAVID R

ART UNIT	PAPER NUMBER
1634	11

DATE MAILED: 10/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/841,157	NISHIGAKI ET AL.	
	Examiner	Art Unit	
	David Gunter	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Informalities

1. The claims are objected to because the steps of Claim 1 are numbered 1-5. In order to avoid confusion, the method steps must be assigned letters a-e to distinguish the steps of Claim 1 from Claims 1-5.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

2. The claims are generally narrative and indefinite, failing to conform to current U.S. practice. They appear to be a literal translation into English from a foreign document and are replete with grammatical and idiomatic errors. The claims must be re-written into idiomatic English.

3. Claims 1, 4, and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Regarding Claim 1, the methods steps lack antecedent basis. The preamble recites "a method for identifying an organism," but the method steps do not result in the identification of an organism. Additional method steps must be added to recite how the analysis of PaSS and/or genome semidistance recited in Claim 1, step 5 results in identification of the organism.

b. Regarding Claim 1, step 1, the phrase "preparing one kind or more of double-stranded DNA fragments" is indefinite because it is not clear what is meant by "kinds" of double stranded DNA. The claim can be read to recite a plurality of double-stranded DNA molecules with distinct sequences or a plurality of double-stranded DNA molecules of the same sequence that possess differences in structure, labels, molecular weight, or other characteristics. The claim must be amended to clarify the nature of the DNA molecules present.

c. Regarding Claim 1, step 3, and Claim 6, the phrase "extracting identification dots of each DNA fragment" is indefinite because the meaning of "extracting" and "identification dots" is not clear. For the purpose of examination, it will be assumed that "identification dots" is synonymous with the "featuring points" described beginning in the third paragraph of page 18 of the specification. However, the claim must be amended to either replace the term "identification dots" with nomenclature recognized in the art, or provide a definition of "identification dots." Furthermore, "extracting" will be interpreted to mean that the featuring points are identified and their position recorded. There is no indication in the Claims that the DNA at these featuring points is physically extracted from the gel for sequencing or other purposes. The claim must be amended to replace or clarify the meaning of "extraction."

d. Regarding Claim 1, step 5, the phrase "a standard DNA is co-existed as a standard point for the identification dots and the pseudo-absolute location of the identification dots is determined" is not clear.

1) For the purpose of examination, the phrase "a standard DNA is co-existed" will be interpreted to mean that a standard DNA sample with known characteristics will be run side-by-side with the sample to be tested. However, the claim must be amended to clarify the meaning of the term "co-existed".

2.) For the purpose of examination, the phrase "pseudo-absolute location of the identification dots" will be interpreted to mean that the results of the electrophoresis of the standard DNA sample will be compared to those of the sample to be tested and the relative location of key features will be measured. However, the claim must be amended to clarify the meaning of "pseudo-absolute location".

e. Regarding Claim 4, the phrase "a raw material labeled with a fluorescent marker" is indefinite because the meaning of the term "raw material" is unclear. The Claim must be amended to indicate which specific material bears the fluorescent marker.

f. Regarding Claims 4 and 5, the abbreviation "PaSS" is unclear. Any abbreviations used in a claim must be spelled out in order to clearly identify the subject matter of the claim. In addition, the mathematical formula for PaSS and genome semi-distance must be specifically recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rolleke, et al., Applied and Environmental Microbiology 62(6):2059-2065. 1996 (hereinafter referred to as "Rolleke") in view of Pena, et al. Proc. Natl. Acad. Sci. USA 91:1946-1949. 1994 (hereinafter referred to as "Pena") in further view of Pleissner, et al, Electrophoresis 20:755-765. 1999 (hereinafter referred to as "Pleissner"). Claim 1 recites a method comprising the steps of (1) preparing double-stranded DNA fragments by a random PCR using as a template at least part of a genome of an organism to be identified, (2) submitting these DNA fragments to either temperature gradient gel electrophoresis (TGGE) or denaturant gel gradient electrophoresis (DGGE), (3) "extracting identification dots of each DNA fragment," (4) determining "PaSS and/or genome semi-distance" from the identification dots, and (5) analyzing the PaSS or genome semi-distance wherein during the electrophoresis by TGGE or DGGE, a standard DNA is used as a reference point to determine the location of the "identification dots."

Rolleke discloses a similar method for identifying an organism in which DNA is extracted from bacteria and amplified by PCR. The resulting fragments are separated by DGGE and the band pattern ("identification dots") generated by the fragments is used to distinguish between organisms (page 2060, left column, sixth paragraph through right column, sixth paragraph). Rolleke does not specifically disclose random PCR, nor does Rolleke disclose two-dimensional DGGE with subsequent mathematical analysis of the pattern of spots generated by the DNA fragments.

Pena discloses a method of preparing double-stranded DNA fragments by random PCR using as a template at least part of a genome of an organism to be identified. The technique disclosed by Pena involves the use of a single PCR primer and a low annealing temperature to generate a repeatable, unique "multiband gene signature" (page 1946, left column) for a DNA template. This procedure is identical to the PCR technique described on pages 3-6 on the instant application. It would have been obvious to one of ordinary skill in the art at the time the application was filed to modify the method of Rolleke to incorporate the random PCR method of Pena instead of more traditional PCR techniques in order to improve the quality of the results from Rolleke's method by providing a consistently repeatable starting material with a unique pattern of DNA fragments for each organism.

As stated above in paragraph 1b under the section heading "Claim Rejections - 35 USC § 112," the meaning of the phrase "extracting identification dots of each DNA fragment" is not clear. For the purpose of examination, it will be assumed that "identification dots" is synonymous with the "featuring points" described beginning in the third paragraph of page 18 of

the specification, and that "extracting" means that the featuring points are identified and their position recorded.

PCR-based methods such as those of Rolleke, Pena, and the instant application produce a pattern of bands or spots based on the migration of the amplified DNA fragments. It was well known to one of ordinary skill in the art at the time the application was filed that there were numerous methods for detecting features present on a two-dimensional gel, and numerous algorithms for comparing features present on a plurality of gels (for a review of techniques available as of 1999, see the discussion in Pleissner beginning on page 758, left column). It would have been obvious to one of ordinary skill in the art at the time the application was filed to modify the method of Rolleke to add the step of separating the amplified DNA fragments based on size prior to DGGE. This additional step was routinely practiced by those of skill in the art, and would allow a more detailed analysis of the pattern of DNA fragments produced by PCR. It would have been further obvious to analyze the data generated by the method of Rolleke, as modified by the inclusion of an additional electrophoresis step, using an algorithm to produce an objective, quantitative description of the data to allow comparisons of the DNA fragment patterns produced by a plurality of organisms. One of ordinary skill in the art would have been motivated to select an algorithm among those taught in the prior art based on experimental design and desired results.

Pleissner does not specifically teach the formula for PaSS disclosed on page 21 of the specification, nor the formula for genome semi-distance disclosed on page 22. However, there are numerous known formulas and algorithms for the comparison of spots on two-dimensional electrophoresis gels. These methods generate a quantitative measure of the degree of similarity

between the pattern of DNA fragments generated by DNA samples (Pleissner, page 764). The method of the current application consists of the steps of methods known in the art (amplification of DNA, DGGE, mathematical analysis of the pattern of DNA spots) for the purpose of accomplishing a result known in the art (comparison of the similarity between spots generated from two DNA samples). Because the steps of the method and the results of the method are the same as the prior art, and in the absence of unexpected results, the method is rejected as unpatentable over Pena as modified by Rolleke and Pleissner. In re Sussman, 141 F.2d 267, 60 USPQ 538, 540-541 (CCPA 1944). In re Spada 911 F.2d 705, 15 USPQ2d 1655 (Fed Cir 1990).

The examiner notes that the use of a standard to serve as a reference point for the measurement of the location of DNA bands was well known to those of ordinary skill in the art at the time the application was filed.

a. Regarding Claim 2, the method of Claim 1 is unpatentable over Pena as modified by Rolleke and Pleissner, as described above. SEQ ID NO: 1 was known at the time the application was filed to be part of the genome of bacteriophage f1 isolated from *Escherichia coli* (GenBank Accession Number J02448, April 1993). It would have been obvious to one of ordinary skill in the art at the time the application was filed to use bacteriophage DNA as a standard based on the prevalence of phage DNA in bacterial genomes and the likelihood that any bacteria to be identified would contain phage DNA. SEQ ID NO: 2 was described in GenBank accession number AE000174, 1997) as a fragment of the genome of *Escherichia coli* K12. It would have been obvious to one of ordinary skill in the art at the time the application was filed to use a portion of the genome of *E. coli* as a standard because of its status as one of the most extensively

studied bacteria and its ready availability in a research setting. Further more, it would have been obvious to one of ordinary skill in the art at the time the application was filed to use a DNA standard of phage (SEQ ID NO: 1) or bacterial (SEQ ID NO: 2) origin with known length, sequence, and characteristics as a reference for measuring the band pattern generated by a sample to be assayed rather than isolating, purifying, and characterizing a previously unknown fragment of DNA for the same purpose.

b. Regarding Claims 3 and 7, the method of Claim 1 is unpatentable over Pena as modified by Rolleke and Pleissner, as described above. Rolleke further teaches that performing DGGE on PCR fragments amplified from the genome of bacteria can identify the species of the bacterium (page 2059, abstract).

c. Regarding Claims 4 and 5, the method of Claim 1 is unpatentable over Pena as modified by Rolleke and Pleissner. The examiner notes that the incorporation of a labeled nucleotide into a PCR reaction to allow detection of the amplified polynucleotide was routinely practiced by those of ordinary skill in the art at the time the application was filed in procedures such as automated DNA sequencing.

d. Regarding Claim 6, the method of Claim 1 is unpatentable over Pena as modified by Rolleke and Pleissner. Pleissner further teaches several pattern recognition algorithms in which the DNA spots generated by two-dimensional electrophoresis are described by their coordinates along the mobility axis and the temperature/denaturant gradient axis (multiple references, beginning with page 758, left column, first paragraph).

Conclusion

6. **No claims are allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David R. Gunter whose telephone number is (703) 308-1701. The examiner can normally be reached on 9:00 - 5:00 M - F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-9212 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

David R. Gunter, DVM, PhD
September 30, 2002

STEPHANIE W. ZITOMER
PRIMARY EXAMINER